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Mr. Chairman, members of the Subcommittee, thank you for the invitation to appear before you today on behalf of Novo Nordisk. I am Marcus Carr, Executive Director for Clinical Research-Hemostasis of Novo Nordisk. In this capacity, I have been extensively involved with the business development, regulatory approval process, and federal procurement issues related to the potential sale of Novo Nordisk's innovative therapeutic treatment, NovoSeven®, for trauma victims. I have been involved with this project since my arrival at Novo Nordisk in March of 2005. I have knowledge of the NovoSeven from a research perspective that dates to the early 1990s, and I have personally used NovoSeven to treat bleeding patients since its FDA approval in the late 90s. I also have extensive experience in treating bleeding patients of all varieties in my roles as an emergency department physician, as Director of the Central Virginia Bleeding Disorders Center at the Medical College of Virginia of Virginia Commonwealth University in Richmond Virginia, as Professor of Medicine and Pathology at the same institution and as a Medical Corp officer in the United States Army being mobilized for Operations Desert Shield, Desert Storm, Noble Eagle, Enduring Freedom and the Kosovo Campaign.

Novo Nordisk is an established pharmaceutical company and a world leader in diabetes care. The company has the broadest diabetes product portfolio in the industry, including the most advanced products within the area of insulin delivery systems. In addition, Novo Nordisk has a leading position within areas such as haemostasis management, growth hormone therapy and hormone replacement therapy. Novo Nordisk manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society.

With a U.S. base of operations in Princeton, New Jersey, Novo Nordisk employs approximately 20,250 full-time employees in 78 countries, and markets its products in the U.S. and nearly 180 other countries. Novo Nordisk's shares are publicly traded on the New York Stock Exchange (symbol, NVO), as well as the stock exchanges in Copenhagen and London.

The Chemical, Biological, Radiological and Nuclear Threat (CBRN) and Countermeasure Needs

The threat of a terrorist attack on the United States involving chemical, biological, radiological, or nuclear weapons is very real. In October 2001, shortly after the 9/11 terrorist attacks on the World Trade Center and Washington, D.C., the mailing of 5 letters containing anthrax killed five people, sickened nearly two dozen, and required prophylactic antibiotic treatment for 32,000 more. Since the 1980s, terrorist organizations have embraced the use of CBRN threats. For instance, in the last 10 years, the Japanese sect of the Aum Shinrikyo cult has attempted an aerosolized release of anthrax from Tokyo building tops, unsuccessfully attempted to obtain Ebola during an outbreak in Africa and released sarin gas into a subway system. Concern continues to mount about the potential use of CBRN agents against U.S. troops and interests abroad, as well against U.S. civilian populations. Even small scale use of these agents has the potential for enormous social and economic disruption and exhaustion of local and national resources needed to combat the threat, treat disease and clean up environmental contamination. Limited availability of funds has driven efforts to better understand the scope of each threat and the consequences of an attack in order to prioritize pursuit of defenses against the highest priority agents. For biological threats, the CDC has identified and classified over 40 agents in Categories A-C. For a vast majority of these agents, there are neither effective preventive vaccines, nor effective antidotes following exposure, or both.

Aside from their ability to inflict great harm, there are significant differences among CBRN agents at the physical and technical level that complicate development of defensive countermeasures, particularly detection systems. Variation from agent-to-agent often mandates tailored strategies specific for a given agent. However, it is similarities among CBRN agents at the symptomatic level too that can hinder development of diagnostic systems. Several national programs exist to monitor and provide early warning in the case of a terrorism event, including BioWatch and BioSense, as well global programs such as the Emerging Infections Sentinel Networks. In addition to screening the environment for the presence of pathogens, a sudden increase in non-specific syndromes may indicate a bioterrorism event. The recognition of a large number of previously healthy individuals with a common site of exposure presenting with similar symptoms including severe respiratory illness with fever, gastrointestinal maladies, encephalitis or meningitis, neuromuscular illness, fever with rash or bleeding disorders could indicate a CBRN attack. However, the development of rapid diagnostics for both known and unknown threats remains a challenge.

Even before a definitive diagnosis is made, greater problems will arise in identifying, isolating and treating a potentially large numbers of victims and such a situation could develop into a crisis. In the case of a CBRN attack, there will likely be difficulty in diagnosing the causative agent, especially since many of the potential threat agents manifest with very similar symptoms. For this reason, it is critical to develop countermeasures that are broadly applicable, especially in the absence of a diagnosis or in the case of a genetically modified or emerging threat. Further, countermeasures that are efficacious in treating a variety of ailments are highly desirable since the nature of future terrorist attacks are unknown.

There are two main strategies to prepare for a CBRN attack. The first is to develop preventatives for the known threat agents (i.e., anthrax and smallpox vaccines). This approach is only effective against a biological attack with previously known and characterized agents. One difficulty with this approach is the ability to vaccinate the entire U.S. population against each and every threat agent. In particular, mass vaccination approaches pose a significant risk/benefit concern with children, elderly, women of child bearing age and immunocompromised individuals. If mass vaccination is not carried out prior to an attack, naïve individuals will be susceptible to the causative agent until vaccinated. To date, anthrax and smallpox are the only biological threat agents with FDA approved vaccines, and these vaccines are associated with certain limitations on their use.

The second key element of an overall medical strategy in preparing for CBRN attacks is the development of countermeasures for post exposure treatment. At this point in time, the therapy following exposure to most of the CBRN threats is largely supportive. Antibiotic therapy can be used for treatment of most of the bacterial agents. There is no approved treatment for any of the hemorrhagic fever viruses. While ribavirin may be used under an Investigational New Drug (IND) protocol for the arenaviruses and bunyaviruses, no such treatment exists for the filoviruses or flaviviruses. Only a few approved therapies exist for exposure to a toxin, chemical or radiation, and treatment is dependent on identifiable symptoms in the individual patient.

Many countermeasures are being pursued that target specific agents. An inhalation form of the antibiotic Ciprofloxin is being developed for a treatment for inhalation anthrax disease. Additional specific measures are at various stages of testing and development for treatment of other CBRN threats--most of which, if successfully developed, will not be available for stockpiling for over a decade. Importantly, a common concern among the government in stockpiling drugs for post exposure treatment is the length of the window after exposure to an agent in which a drug can be administered and still be efficacious. The window of criticality in which treatment must occur may be very narrow. Often a definitive diagnosis is needed to decide upon an appropriate countermeasure to administer. The period of latency before symptoms emerge that is associated in particular with biological agents adds a significant hurdle in that without adequate diagnostic tests to detect disease in early stages, by the time the patient exhibits identifiable symptoms, the drugs under development may prove ineffective.

Therefore, countermeasures that address common symptoms of CBRN agent exposure will be a necessary addition to the arsenal of treatments for future protection of the U.S. population. We should be able to medically counter each CBRN threat to some measure and degree, but the current state of technology is inadequate for the breadth of threats faced by the U.S. This leaves us highly unprepared to deal with the casualties following a CBRN attack.

NovoSeven

This is where our company's revolutionary new drug, NovoSeven, enters the national medical preparedness picture. But first, let me be clear about one thing to the committee today. The primary focus of Novo Nordisk has *not* been the development of drugs to protect against attack by CBRN weapons. The principal focus of our company has been, and remains, pursuit of

innovative bio-pharma products for the commercial market. We are not a "biodefense" company as that term has come to be known in the post-9/11 environment. While we will certainly work diligently to supply NovoSeven for whatever purpose the US Federal Government feels appropriate, our business plan, our executives, and our investors do not see the primary focus of Novo Nordisk , now or in the future, to be the federal market place.

Nevertheless, in the years since the horrific 9/11 attacks and the ensuing threats which our country faces everyday, we have come to realize that one of our commercial products would be a great asset to the national defense, and we at Novo Nordisk have keenly watched the implementation of Project Bioshield for use as a potential contracting vehicle with the federal government. NovoSeven, is a mature medical therapy with FDA approval for use in hemophilia patients, but it could be also be used to save lives in a CBRN attack by treating bleeding disorders caused by a wide array of threat agents. The immense value of NovoSeven as a life-saving therapy for CBRN applications lies in its unique mechanism of action to prevent severe blood loss and extend the window of opportunity for therapeutic intervention. Availability of NovoSeven would make an immediate contribution to enhancing our nation's medical and public health readiness for mass casualty events. Moreover, the current commercial use of NovoSeven offers an attractive cyclic stockpiling concept in which the drug could be rotated out of the SNS for use in the commercial sector before it expires and be replenished with fresh product. To realize these benefits, Novo Nordisk is positioning NovoSeven as a key component of the comprehensive national plan for readiness against a CBRN attack and as a key asset to the SNS.

Since it reached the general market in 1996, over 700,000 doses of NovoSeven have been administered. NovoSeven is currently only approved by the FDA for use in hemophilia A and B patients and is 80-90% effective in treating bleeding episodes. NovoSeven is also approved for use in treating bleeding episodes in acquired hemophilia, Factor VII deficiency and Glanzmann's thrombasthenia in the European Union. Other reported uses in normal patients include individuals with trauma or surgery-associated hemorrhage, intracerebral and pulmonary hemorrhage, or bleeding following bone marrow transplantation. Phase three pivotal trials to support applications for indications in the areas of intracerebral hemorrhage and trauma should begin this calendar year in the US, Canada and Europe. An application for FDA approval for the use of NovoSeven in inhibitor patients requiring surgery is currently pending. Plans are being prepared for a discussion with the FDA on the most appropriate pathway for approval of NovoSeven in pulmonary hemorrhage. Novo Nordisk currently holds IND protocols for other uses of NovoSeven including treatment of bleeding in trauma patients and also thrombocytopenia following chemical or radiological exposure.

NovoSeven has an excellent safety profile, since it is a recombinant product and contains no human products. To produce NovoSeven, the gene for human Factor VII was cloned and expressed in baby hamster kidney cells. The recombinant protein is secreted into the media of the cells from which it is purified using a chromatographic purification process. The purification process has been demonstrated to remove any potential contaminating viruses. Further, no human serum or other proteins are used in the manufacturing of this product.

NovoSeven has been found to be safe and effective in both patients with bleeding disorders and those without pre-existing coagulopathy. Even following repeated administration, there is no evidence of antigenicity, or immune responses to the product, in patients receiving

NovoSeven. NovoSeven has been shown to be effective when other treatments fail, are contraindicated, or blood products are unavailable. NovoSeven has a very low frequency of serious adverse events, remaining around 1% following administration of greater than 700,000 doses. Even when very high 'mega' doses of the drug are administered, it appears to be safe. The most important serious adverse event type for NovoSeven is thromboembolic (i.e. serious blood clotting) events; however, only 104 thromboembolic events have been reported following administration of more than 700,000 doses of NovoSeven. This represents an event rate of two thromboembolic events per 10,000 standard NovoSeven doses – a very low frequency considering the clinical severity of diseases in which NovoSeven is being used. Of further importance, the mode of action of NovoSeven localizes the coagulation effects to the area of injury, thus avoiding systemic activation of clotting and the risk of thrombosis.

Procurement of NovoSeven under Project Bioshield

Many companies have the capability to develop new products to protect against attack by biological and chemical weapons or other dangerous pathogens. A few firms, such as Novo Nordisk, have already done so. In fact, Novo Nordisk is, by far, among the largest and most qualified companies prepared, as I come before you today, to express interest in Project Bioshield to date. Should Novo Nordisk ultimately prove successful in negotiating a viable business relationship with the federal government to purchase NovoSeven, it will send an extremely powerful, positive signal to similarly qualified companies to enter this marketplace. Of course, failure by Novo Nordisk in this endeavor could have a negative effect on the goal of stimulating greater interest of large biopharma companies.

A great potential exists with NovoSeven, which can be immediately tapped for filling current shortfalls in our medical defense arsenal. NovoSeven may have broad application against bleeding disorders caused by a chemical, biological, radiological or nuclear attack. The use of NovoSeven might be particularly useful in the immediate time period following a CBRN attack occurs--before confirmed diagnosis of the attack agent or in the case of unknown diagnosis. Further, NovoSeven could be a critical component of the SNS for treatment of diseases, such as the hemorrhagic fever viruses, that have no other treatments. NovoSeven could also be useful in combination with other therapies in difficult patient cases or with genetically modified or emerging threats for which treatment is unknown. NovoSeven will also likely be used by health care providers in patients that have not received the proper treatment in time to stop the severe end-stage bleeding disorders associated with CBRN attacks. Additionally, even where there is a definitive diagnosis, cessation of bleeding would be a valuable and necessary component of a combination of treatments to enhance survival in victims with hemorrhagic symptoms.

Proposed Implementation Improvements

Recognizing the need to protect its citizens, the U.S. government is committed to spurring CBRN medical countermeasure development through policy means. The Project BioShield Act of 2004 provides new and necessary tools to improve medical countermeasures protecting Americans against a CBRN attack.

Although Project BioShield is a commendable first step, a number of issues concerning BioShield and the SNS deserve further attention. More specifically, the current implementation scheme for BioShield can be improved upon to maximize the authorities granted through the legislation and to more rapidly and effectively bolster the SNS. First, the procurement of countermeasures is limited by the current implementation scheme because there must be a call for material threat assessments against a specific agent, followed by a call for a countermeasure against that threat. Unfortunately, this process may not be amenable to countermeasures that are effective for treatment of multiple threats.

Further, the current procurement process precludes products with a significant commercial market. This provision of the legislation serves as a disincentive to companies with marketable products with potential broad applications in the CBRN arena (e.g., broad spectrum antibiotics) and deters their participation in CBRN medical countermeasure research and development. It is likely that mature technologies exist which are approved for other uses but could also provide *near-term* solutions to the country's CBRN defense needs if given the opportunity to compete for Project BioShield contracts. Pursuing FDA-approved drugs for other CBRN related indications could significantly expedite the regulatory and development process since these products have already been used in humans.

Many of the specifically targeted countermeasures are in such early stages of development that it will be years before they can be stockpiled under IND status and then subsequently licensed. Addressing these issues as soon as possible will allow for the acquisition of broad-acting therapeutics that may already have a commercial market. Thus, BioShield could fulfill its intent to establish a stockpile of vaccines and therapeutics to counter various CBRN agents by serving as a mechanism to spur development of specific countermeasures, while simultaneously encouraging the pharmaceutical industry to consider the use of their current drugs for treatment of CBRN induced diseases or syndromes. Our nation should focus first on acquiring the most mature products now, while still promoting an innovative pipeline of countermeasures, thereby stockpiling a broad range of products that defend against immediate and future threats.

In closing, I believe what I have outlined today represents good, sound public policy--both in terms of enhancing our homeland security greatly, while allowing for the most industrious use of U.S. taxpayer dollars. Thank you again for this opportunity to testify today. I look forward to hearing the committee's thoughts and answering any questions the members may have.